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CHANGES IN SENSORY RESPONSIVENESS IN BEHAVING PRIMATES

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(U) TENNESSEE UNIV MEMPHIS DEPT OF ANATOMY AND

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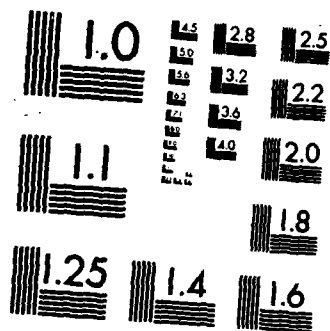
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Research Objectives - Statement of Work-

In this first year, our three main goals were to establish a functional behavioral neurophysiology laboratory at the University of Tennessee-Memphis, to train monkeys to perform hand movements in response to both visual and vibratory go-cues, performing these movements at reaction time latencies, and to begin recording from the sensorimotor cortices of at least one of these animals to investigate the changes in sensory responsiveness to inputs from the hand that will subsequently be moved, during the initiation and execution of wrist movements.

Establishment of the laboratory:

Establishing a functional laboratory has required the purchase of several pieces of research equipment, the fabrication of others which are specific to this project and unavailable on the common market, and the integration of these materials and devices with existent instruments to allow computer-controlled behavioral training and monitoring, and electrophysiological recording in awake, behaving monkeys. All research equipment listed in the original proposal has been purchased, with the exception of the paper chart recorder. A microcomputer has been substituted for this item with prior approval of AFOSR. The laboratory became fully functional in January 1986. Concentrated behavioral training of the first monkey was begun at this point and the second began training in March.

Behavioral Training:

Two adult rhesus monkeys (*Macaca mulatta*) have been trained to flex or extend their wrists in response to a visual cue or to a vibratory cue presented to the volar surface of the same hand that was subsequently moved. A display panel indicates the current wrist position to the animals by a single, large red light emitting diode (LED) indicating the center position and banks of smaller, vertically oriented LEDs indicating successive 1 degree deviations from the center position. Visual go-cues for movement are indicated by shifting the position the animals' feedback of current wrist position a number of lamps in the opposite direction from the movement that is to be requested. The animals have been trained to make movements in response to these lamp shifts. Vibratory stimuli are delivered to an animal's hand via a smooth, flat plate on which the monkey's hand rested. This plate is attached to the axle of a DC torque motor that applies a constant torque of 0.07 Nm in the upward direction. Each trial begins when the monkey positions the plate in a centered position. The animal must maintain this position for either 0.75, 1.0, 1.25 or 1.5 seconds (computer randomized). Deviation of wrist position greater than 0.5 degrees during

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this period cancels that trial. If the animal successfully maintains position for the appropriate time, a vibratory go-cue (either 27, 57 or 127Hz; presented in blocks of 80 trials each) or a lamp shift is presented and remains in effect until the animal moves the manipulandum at least 5 degrees from the centered position; then it is turned off. Each monkey receives a fruit juice reward for movement in the appropriate direction. The instruction for the direction of vibratory triggered trials is a LED in the upper left corner of a display panel. When illuminated, it requests extension, otherwise flexion upon go-cue receipt. Visually triggered trials are presented randomly in each block of trials and indicated by another, different colored LED. Flexion and extension movements are requested in alternating blocks of ten trials each. The instruction stimuli are constantly present throughout each trial. Whether the monkey fails or is rewarded for each trial, the next trial begins when the animal repositions the manipulandum in the center zone. Figure 1 illustrates the basic behavioral paradigm. The time between the onset of the go-cue and the actual movement onset is defined as the reaction time. Data concerning the animal's performance and the difference between visual and vibratory reaction time is presented below.

Surgical preparation:

The first monkey had sufficiently mastered the behavioral task by early May and surgical implantation of the devices necessary for chronic electrophysiological recording from the sensorimotor cortices was conducted on May 21. Under general anesthesia, a craniotomy was performed over the pre- and postcentral cortices. A surgically implantable-grade stainless steel (316-L) chamber was implanted over the opening. The chamber is necessary to allow access to the cortical structures below and to hold a stereotaxic device that allows passage of recording electrodes into the brain. The dural covering of the brain was left intact. Four mounting bolts were implanted in the skull to hold a head restraint device. These and the chamber were cemented in place with surgical methyl-methacrylate. The wounds were closed in layers and systemic antibiotics given. The animal recovered within 6 hours and behavioral testing was begun a week post-operatively. Within two weeks, the animal's behavioral performance was judged to be similar to his pre-operative behavior and electrophysiological recording experiments were begun.

Each day, transdural penetrations are made into the cortex with glass-coated platinum-iridium microelectrodes having an impedance of 0.9-1.4 megaohms at 1KHz. Extracellular recordings are made of the activity task-related neurons during the animal's performance of the behavioral task. Single-unit activity is discriminated by passing the amplified signal of the neuronal discharge through a window discrim-



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inator and selecting only the action potentials from a single neuron. This information is digitized by a microcomputer as is the position of the animal's hand during the performance of the behavioral task. This strategy allows us to correlate changes in the animal's behavior, specifically the movement of the hand, with changes in neuronal firing patterns associated with that movement or the presentation of either of the go-cues. When possible, the peripheral receptive field (RF) of each neuron is examined by stimulating glabrous surfaces with a hand-held probe, manipulating hairy skin surfaces and joints and palpating forelimb muscles. In addition, the frequency of the vibratory go-cue is changed to determine if there are changes in sensory responsiveness related to stimulus frequency during the performance of these tasks and thus allowing us to determine the optimal frequency for the presentation of information without hindering the animal's ability to successfully perform the task.

Status of the Research-

This project was proposed initially because our preliminary studies indicated that there are at least two distinct types of changes in sensory responsiveness that are associated with the initiation and execution of movement of the same hand that senses the peripheral go-cue. We observed two types of activity changes in primate primary somatosensory cortex (SI) neurons. It is this region of the cerebral cortex that is the recipient of information about the sense of touch and of limb position, both of which are necessary for the accurate and expedient adjustments required of a subject that is controlling any sort of mechanical device with his hand. In monkeys, both types of changes in sensory responsiveness of SI neurons appear to depend on the animal's behavioral state. Subsequent motor adjustments of hand position resulting from motor commands programmed in higher centers of the brain must derive their information about the current state of the forelimb from signals relayed through these cortical regions. If information about the periphery is subject to changes in sensory responsiveness, i.e., is sometimes available and sometimes attenuated during the initiation and execution of hand movement, then it is important to know the timing of the normal mechanisms involved in sensory perception to most efficiently provide the subject with the information that will result in the successful completion of the motor behavior.

The first type of change in sensory responsiveness observed depended on the behavioral context in which the peripheral stimuli are presented. Changes in firing rate time-locked to the stimulus onset when it serves as the go-cue for hand movement did not occur when the monkey previously was instructed not to move. A second type, which preceded movement onset, was observed for some SI neurons initially exhibiting increased

discharge rates with vibratory peripheral stimulation. This type showed a activity decrease occurring 70-90ms before movement onset. This decrease was termed pre-movement suppression (PMS) and its timing corresponded to previous psychophysical observations of increased tactile threshold before movement. Thus, pre-movement suppression may be the neural correlate of the increased tactile threshold observed before the hand that was stimulated is moved.

Both types of activity changes were observed in SI neurons that exhibited short latency (<30ms) firing rate alterations following the onset of a vibratory go-cue. We next sought to determine if other SI neurons, e.g., those that did not respond to the go-cue, also change activity prior to movement onset and at the same time as those exhibiting PMS. We found that a significant percentage, about 20% of the task-related SI neurons exhibited some sort of pre-movement changes in firing rate that preceded movement onset.

We then wondered if similar changes occurred if the trigger stimulus was visual rather than somatosensory. If pre-movement changes occur for movements begun by either cue, then this would suggest that this type of change in sensory responsiveness is a generalized feature of sensorimotor behavior in primates and can be generalized to motor behaviors executed by human subjects. In addition, it was observed that the reaction time for movements triggered by vibratory cues were somewhat less than those normally reported for movements made in response to visual stimuli. This suggested that it may be possible to cause subjects to react more quickly to situational changes if informational cues were presented by vibrating the hand rather than by presenting information visually. Since each monkey must be trained to perform both visual and tactile triggered movements, we have an opportunity to examine this contention directly by comparing the reaction times for movements following each type of go-cue.

Visual vs. vibratory reaction times:

Figure 2 illustrates the learning curves that were generated from the behavior of the first monkey. The mean reaction time for flexion and extension movements, triggered by either lamp shifts (visual) or vibration to the surface of the hand, are plotted. Initially there was a wide variance in mean reaction time from day to day for any of the four conditions illustrated. In general, however, reaction times for movements made in response to vibratory cues were less than those for visual cues.

As the monkey became more consistent in his behavior (at sometime after day 45), a constant trend emerged. Visual reaction times appeared to be on the order of 70-100 msec greater than those for vibratory

trials, independent of the direction of the intended movement. This trend was maintained until the day prior to surgical implantation of the recording chamber (day 105) and continues now as we record from cortical neurons as the animal performs the tasks. The mean reaction time for vibratory triggered flexion and extension movements was about 280 msec, whereas those for visually triggered flexion and extension were 350 msec and 380 msec, respectively. It appears that there is at least a 70 msec difference in the monkey's ability to begin movements after vibratory information is delivered as compared with visual information.

This difference may be due in part to the time required for retinal processing of a visual image, which is about 40 msec, and in part to the assumption that several visual cortical regions must be passed through in order to transmit this information to cerebral control centers involved in formulating the movement commands. The latency at which visual input reaches the first cortical processing region is about 60 msec, whereas the transmission of input from the hand to the cortex can be as short as 11 msec. We have not completed training of the second monkey at this date. However, we have no reason to expect any differences, rather we expect great similarities in his performance.

These results suggest that if a requirement for necessary behavior is to process a warning signal and react as quickly as possible with some corrective measure, vibratory signals may result in faster reaction to the situation. More investigation is needed, however, because we have found previously, as have others before us, that vibration of the hand, under some circumstances, can interfere with the discharge of cortical neurons that receive input from peripheral sensory receptors that encode the position of the wrist. Thus, it will be necessary to determine the normally occurring changes in sensory responsiveness to insure that stimulus presentation occurs in a manner that does not degrade motor performance.

Electrophysiological recordings:

Figures 3 and 4 illustrate the firing patterns of a sensorimotor cortical neuron recorded during the monkey's performance of both vibratory and visually triggered movements, as well as the animal's changes in hand position as a result of the requested movements. In the upper panels of each figure, both the neuronal discharge records and the hand position records are centered on the onset of the trigger stimulus (either vibration at 57Hz or lamp shift in figures 3 and 4, respectively). The lower panels in each figure show the same behavioral trials, centered, in this instance, on movement onset. This neuron responded to passive extension of the wrist.

These figures detail several interesting observations: 1) This sensorimotor cortical neuron did not respond to the vibratory go-cue at short latency (≤ 30 msec) before either flexion or extension movements (fig. 3, upper panels, after arrow). 2) There was a decrease in discharge at about 40 msec after visual stimulus onset (fig. 4, upper right panel), but it seems unlikely that this decrease is due to the lamp shift because the latency is too short to be cortically mediated. 3) In both flexion and extension trials for vibratory triggered trials, this neuron decreased firing rate at about 80 msec after go-cue onset (fig. 3, upper panels). No consistent change in firing rate was observed for the visually triggered trials (fig. 4, upper panels). 4) At about 100-110 msec before movement onset for both trials triggered by vibration and those triggered by lamp shifts, there was a dramatic increase in firing rate, observed only when the monkey subsequently performed flexion movements (figs. 3 & 4, lower right panels, respectively). 5) These pre-movement changes in activity are closely associated with movement onset for both types of trials, despite the fact that the reaction time, (that interval in the upper panels of each figure, located between the centering arrow and the dark marks in the raster record), for visually trigger movements is significantly greater than that for vibratory triggered movements.

From this type of data, we may infer that: 1) The neuron's uni-directional pre-movement increase in activity is associated with the onset of flexion movements, regardless of the type of go-cue that signals that the movement may be initiated. 2) The timing of this increase is relatively the same for both conditions. 3) In no instance does this neuron respond consistently to the go-cue, be it either lamp shift or vibration, at short latency (≤ 30 msec for vibration and between 60 and 90 msec for lamp shift). 4) For trials in which the go-cue is vibration, there is a longer latency (~ 80 msec) change in firing rate, which does not occur in visually-triggered trials. In this instance, this observation suggests that while the pre-movement activity changes for vibratory and visually triggered movements are the same, there is a change in responsiveness of this neuron that occurs only in trials that have a vibratory go-cue.

To date we have made 14 penetrations into the sensorimotor cortex and recorded from 18 task related neurons. This is but the beginning of our examination of this animal. Once many more penetrations are made and we have a large population of these neuronal records, more definitive statements can be made regarding the neuronal basis for changes in sensory responsiveness in sensorimotor cortical neurons and the relationship of pre-movement activity changes to movement, the type of triggering information and its effect on neuronal discharge and the normal characteristics of cortical information processing during

movements initiated in response to peripheral input and designed to control devices with the hand.

Listing of Written Publications-

- R. J. Nelson. Activity of postcentral somatosensory cortical neurons changes prior to active movement. Neuroscience Abst. 11:752, 1985.
- R. J. Nelson. Activity of monkey primary somatosensory cortical neurons changes prior to active movement. Brain Res. (submitted, July, 1986).
- R. J. Nelson. Sensory responsiveness of monkey primary somatosensory cortical neurons prior to vibratory stimuli presented before active hand movement. (for Exp. Brain Res., In preparation).
- R. J. Nelson. Changes in sensory responsiveness of monkey primary somatosensory cortical neurons prior to active hand movement. (for Exp. Brain Res., In preparation).

Associated Personnel-

Michael D. Fromke:

On 28 July 1985, Michael D. Fromke was hired as a Research Assistant with a full-time commitment to this research project. Mr. Fromke, a recent graduate of Wheaton College, has since become proficient in all technical aspects required in his position, including animal training, electronics fabrication, on-line data collection and off-line data analysis. Mr. Fromke will be leaving in September to begin Medical School. A replacement is currently being sought for his position.

Matthew W. Wood, Jr., M.D.:

Matthew W. Wood, Jr., M.D. joined the laboratory on 2 January 1986. Dr. Wood is a neurosurgical resident who is fulfilling the laboratory experience portion of his training in this laboratory. He is sponsored by the Neuroscience Center of Excellence Grant awarded to the University of Tennessee- Memphis by the state government, and has, in the short time he was with us, become familiar with all aspects of the functionings of this laboratory. He was of great benefit in the surgical procedures and in extracellular single-unit cortical recording. Dr. Wood left the laboratory at the end of June to become the Chief Resident in Neurosurgery at the University of Tennessee- Memphis Health Sciences Center.

Steven L. Klein, M.D.:

Steven L. Klein, M.D. joined the laboratory on 1 July 1986. Dr. Klein is also a neurosurgical resident and has been chosen to fulfill his laboratory experience in this laboratory. He is supported by the Department of Neurosurgery at U.T. Dr. Klein is somewhat unusual in that he has had previous experience recording from awake, behaving monkeys. The experience stems from a project he participated in as an undergraduate at the University of Washington- Seattle and involved recording from motor cortex in normal and epileptic monkeys. He will be with us for 3-6 months.

Interactions-

Papers presented at meetings:

Activity of postcentral somatosensory cortical neurons changes prior to active movement. Presented at Society for Neuroscience, 15th Annual Meeting, Dallas TX, October 22, 1985.

Ad Hoc Reviewer:

Journal of Neurophysiology - reviewed two manuscripts for publication.

Veteran's Administration - reviewed one scientific proposal.

New Discoveries-

None.

Other Statements-

Included with this Annual Technical Report is a copy of a manuscript that we intend to submit to Brain Research this month (July '86). The work described therein was conducted while I was a Staff Fellow at the National Institute of Mental Health. The analysis, however, was done during the this grant period and the results are pertinent to the project. Therefore it has been included with this report.

Figure Legends-

Figure 1.- Schematic illustration of the behavioral tasks. The monkeys must center the handle and maintain this position until they receive either a vibratory or visual go-cue. They must then either flex or extend their wrists in response to this cue. Task described fully in text on pages 1 and 2 (behavioral training).

Figure 2.- Learning curves for flexion and extension movements triggered by either visual or vibratory go-cues. Mean reaction time for each type of trials during the testing day on the abscissa. The ordinate is day of training. Note that movement in visually triggered trials occurs at greater latency than that for trials begun with a vibratory trigger stimulus.

Figure 3 - Discharge patterns of a sensorimotor cortical neuron recorded during the performance of the behavioral task. Each panel consists of a raster display of the neuronal firing, in which each dot represents a single spike and each row a single trial, a histogram that sums the activity for all trials in 10 msec bins, displayed as the mean discharge rate per bin in spikes per second, and the positional changes associated with each trial above, as well as the average position record. Both extension trials (left panels) and flexion trials (right panels) are centered on the onset of the vibratory go-cue (**arrows**, upper panels) and on the onset of the movement (**arrows**, lower panels). Darker **marks** in the raster displays indicate movement onset (upper panels) or the time when the handle position deviated 5 degrees from the hold position and the time of delivery of the reward (lower panels). Trials are displayed in increasing order with respect to reaction time (upper panels) or the time from movement onset to time of 5 degree movement (lower panels). Full sweep is 2 sec; time bar indicates 200 msec. This neuron increased firing with passive wrist extension. Activity changes occurred about 100 msec before active flexion movements.

Figure 4 - Format as in figure 3 with the exception that in the upper panels, both records are centered on the onset of the lampshift that served as the go-cue for extension (left panels) and flexion (right panels) movements. Lower records are centered on movement onset.

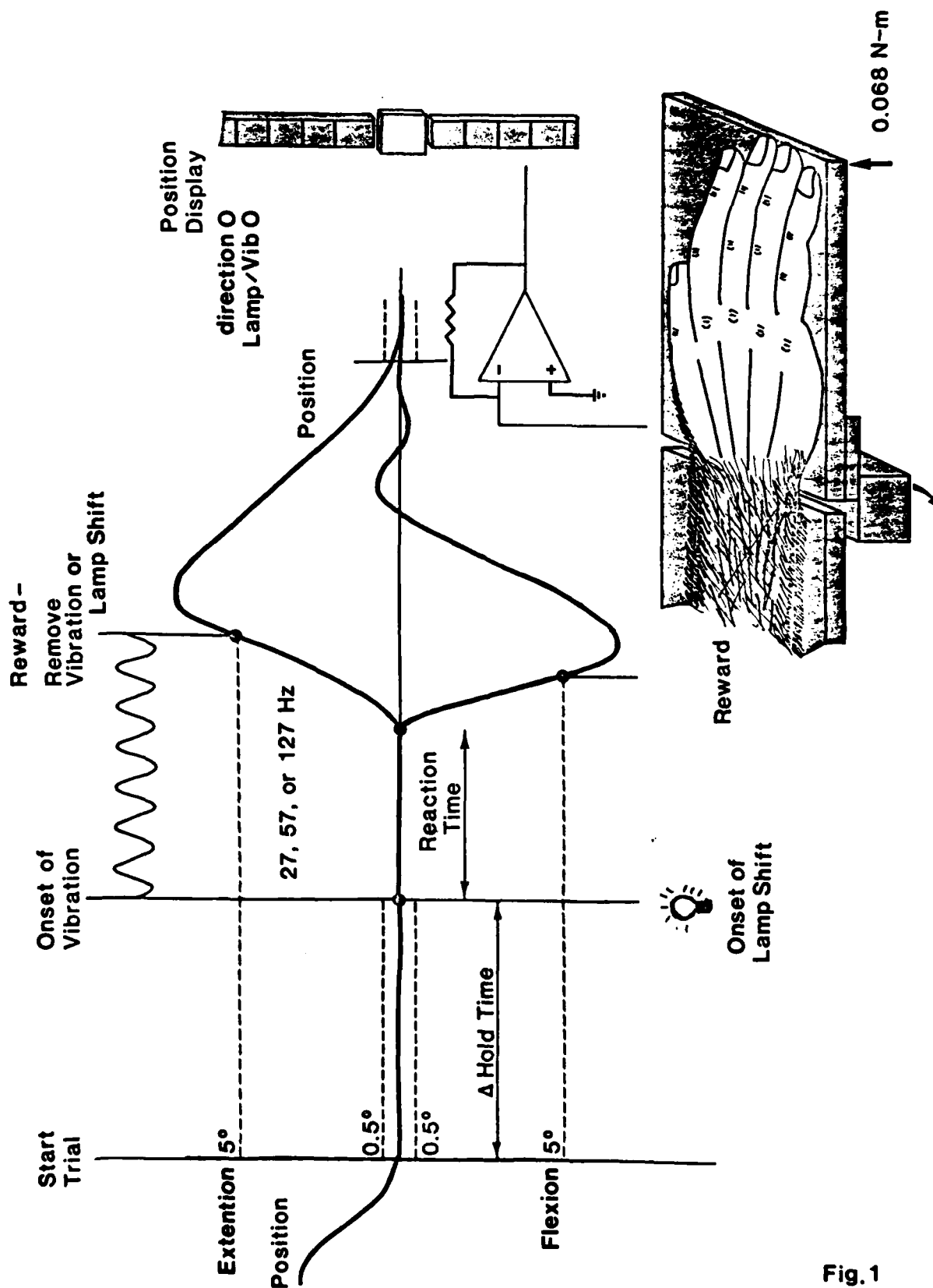


Fig. 1

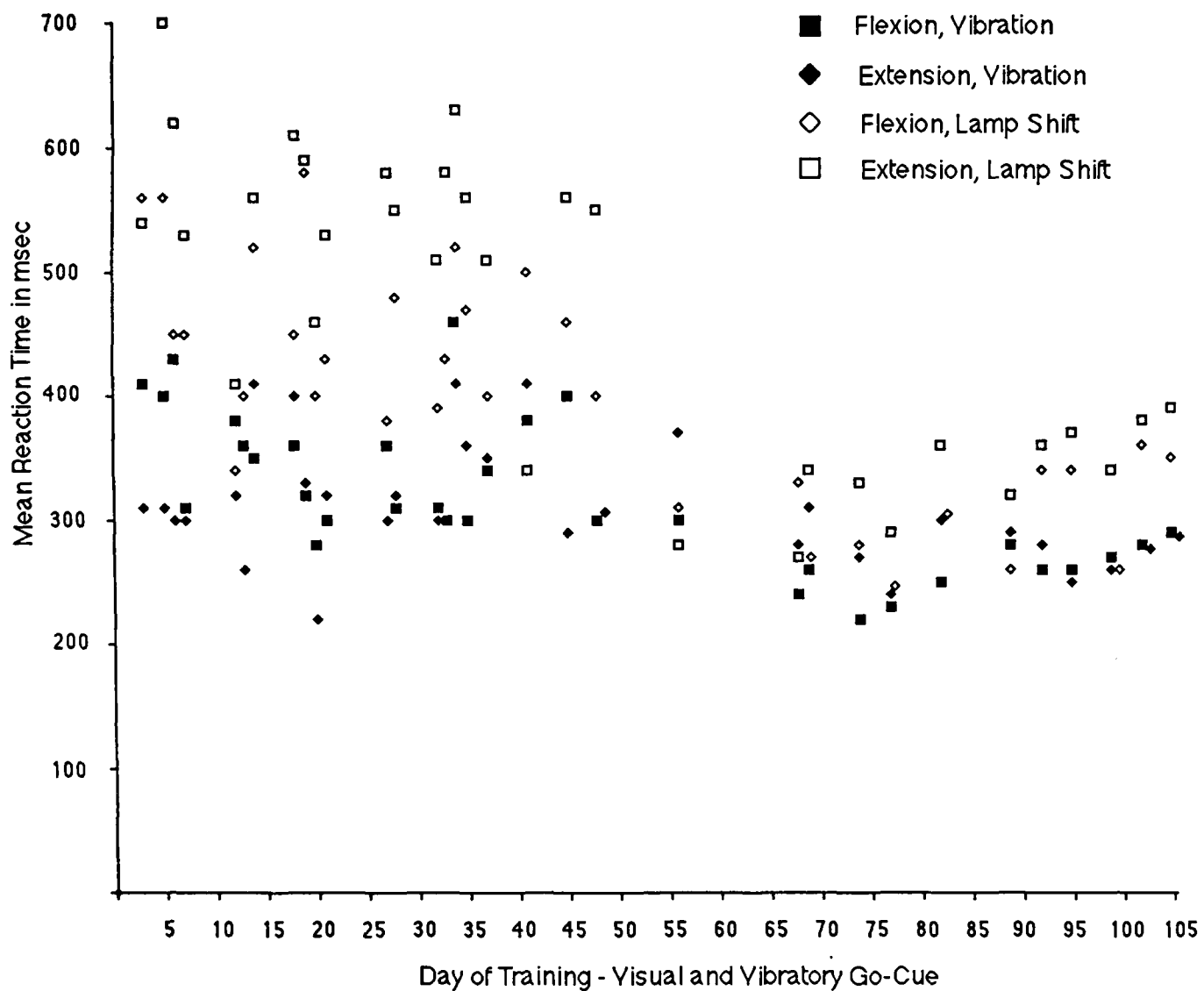
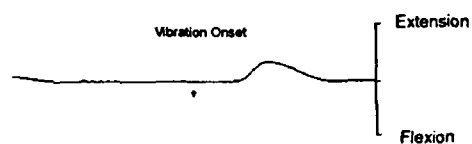
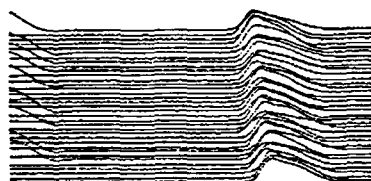
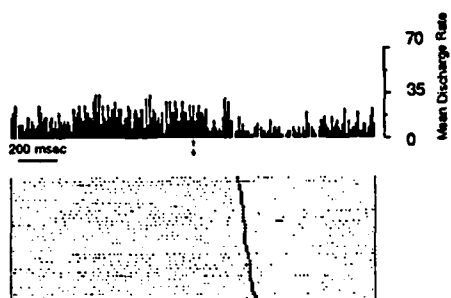


Fig. 2

Extension



Flexion

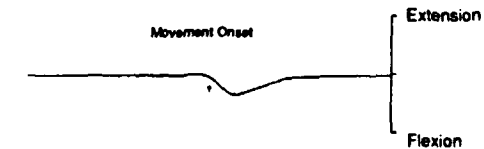
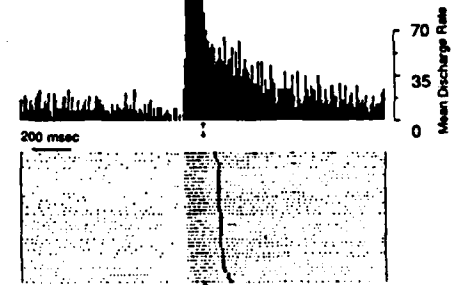
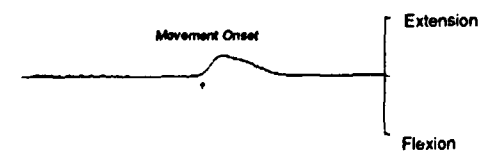
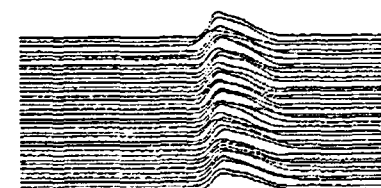
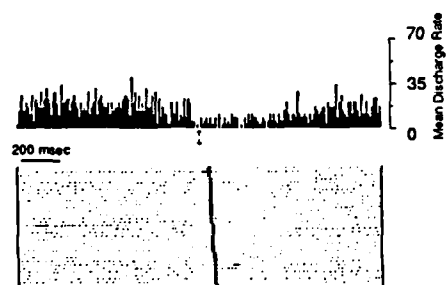
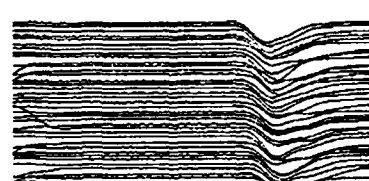
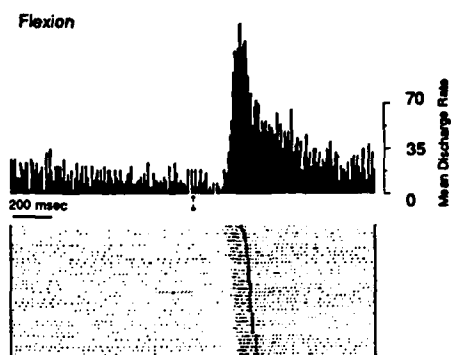
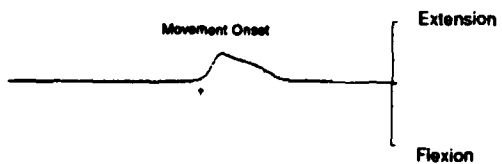
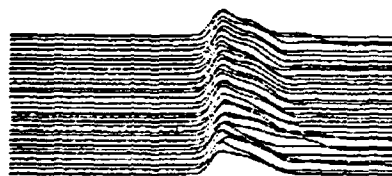
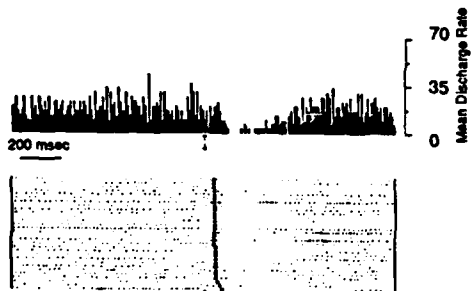
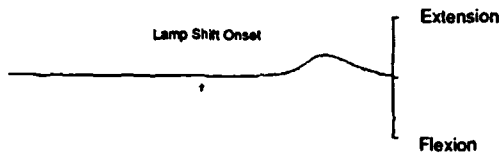
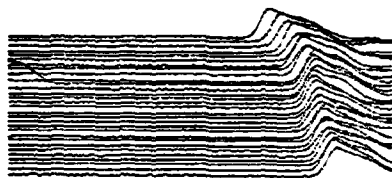
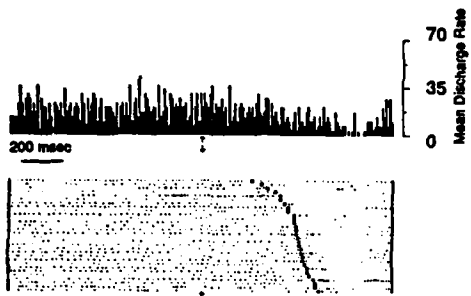
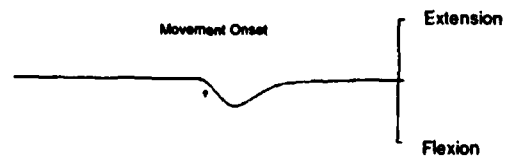
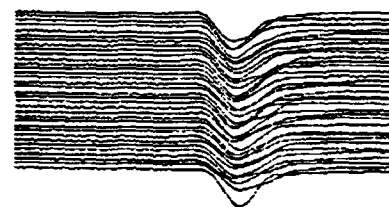
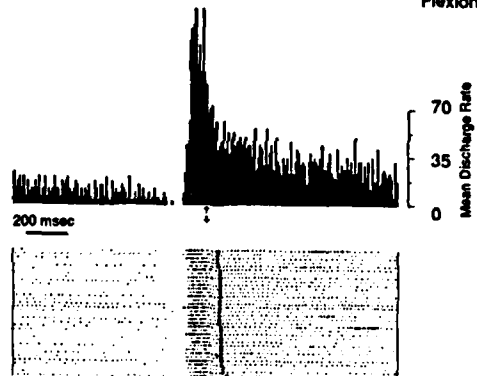
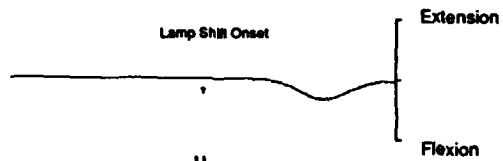
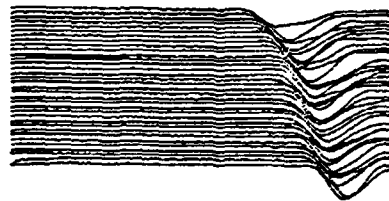
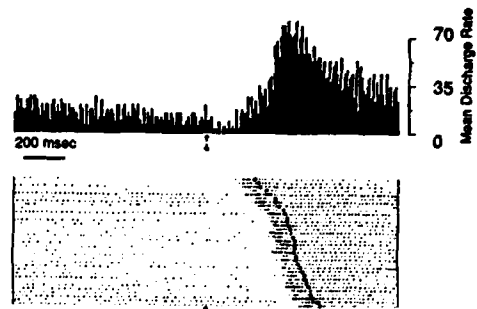


Fig. 3

Extension



Flexion



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